I. AMENDMENT

IN THE SPECIFICATION

Please replace the paragraph beginning on page 3, line 15, with the following rewritten paragraph:

-- In part because of their potential as therapeutics and diagnostics, many groups have reported the generation of monoclonal antibodies to CD23. See, e.g., Rector et al., *Immunol.*, 55:481-488 (1985); Suemura et al., *J. Immunol.*, 137:1214-1220 (1986); Noro et al., *J. Immunol.*, 137:1258-1263 (1986); Bonnefoy et al., *J. Immunol.*, 138:~~2170-2178~~ 2970-2978 (1987); Flores-Romo et al., *Science*, 261:1038-1046 (1993); Sherr et al.; *J. Immunol.*, 142:481-489 (1989); and Pene et al., *Proc. Natl. Acad. Sci., USA*, 85:6880-6884 (1988). Moreover, as discussed *supra*, the usage of such antibodies specifically to inhibit IgE production in systems where IgE synthesis is cytokine (IL-4) induced has also been reported. (Flores-Romo et al (*Id.*); Sherr et al. (*Id.*); Bonnefoy et al. (WO 8707302); Bonnefoy et al. (WO 8707302); Bonnefoy et al. (WO 9612741)); Bonnefoy et al., *Eur. J. Immunol* 20:139-144 (1990); Sarfati et al., *J. Immunol* 141:2195-2199 (1988) and Wakai et al., *Hybridoma* 12:25-43 (1993). Also, Flores-Romo et al. (*Id.*) disclose that Fabs prepared from anti-CD23 antibodies inhibit antigen-specific induced IgE responses *in vivo* in the rat. However, notwithstanding what has been reported, the mechanism by which anti-CD23 antibodies modulate IgE expression and in particular, the manner by which they block IL-4 induced IgE production remains unclear. --

Please replace the paragraph beginning on page 5, line 14, with the following rewritten paragraph:

-- Therefore, it has been proposed that the CD21-CD23 interaction may be involved in antigen presentation and subsequent IgE production. Models suggest CD21 on B cells sending an activation signal for IgE production after binding to CD23 on activated T cells present primarily in atopic individuals. (~~Leconant~~ Lecoanet et al., *Immunol.*, 88:35-39 (1996); and Bonnefoy et al., *Int. Amer. Allergy Immunol.*, 107:40-42 (1995).) Blocking this interaction with an anti-CD23 could block induced IgE production. (Aubry et al., *Nature*, 358:505-507 and *Immunol.*, 5:944-949 (1993); Grosjean et al. ~~(1992); Bonnefoy et al.~~, Curr. Opin. *Eur. J. Immunol.*, 24:2982-2988 (1994); Henchoz-Lecoanet et al., *Immunol.*, 88:35-39 (1996) Nambu et al., *Immunol. Lett.*, 44:163-167 (1995); Bonnefoy et al., *Int. Amer. Allergy*

Immunol., 107:40-42 (1995).) It is also possible that antigen presentation is upregulated by CD23 on antigen presenting B cells binding to CD21 on T cells. –

Please replace the paragraph beginning on page 14, line 6, with the following rewritten paragraph:

-- FcγRI is the only one of the three having an appreciable affinity for IgG. It binds both monomeric gamma-1 and gamma-3 with a K_a of about 5 X 10^8 M^{-1}. However, its affinity for human gamma-4 is about 10-fold less, and it does not bind human gamma-2 at all (Fries et al., 1982, J. Immunol. 129: 1041-1049; Kurlander and Batker, 1982, J. Clin. Invest. 69: 1-8; Woof, ~~1986~~ 1984, G. Mol. Immunol. 21: 523-527; see also Burton and Woof, 1992, Human Antibody Effector Function, Adv. Immunol. 51: 1-84). --

Please replace the paragraph beginning on page 15, line 26, with the following rewritten paragraph:

-- More specifically, and as described in greater detail *infra*, five primate monoclonal antibodies which specifically bound both cellular and soluble CD23 were isolated from an Old World monkey (macaque) according to the methodology which is disclosed in commonly assigned Application Serial No. 08/379,072 ~~(now allowed)~~ which issued as U.S. Patent No. 5,658,570 on August 19, 1997, and which ~~application~~ is incorporated by reference in its entirety herein. This application described in detail a means for producing monoclonal antibodies to desired antigens, desirable human antigens, in Old World monkeys and their advantages in relation to antibodies of other species as therapeutics, for example reduced or potentially lack of immunogenicity in humans because of the phylogenetic closeness of humans and Old World monkeys. In fact, because of the phylogenetic closeness of these species, it is difficult to distinguish Old World monkey immunoglobulins from human immunoglobulins by sequence comparison. --

Please replace the paragraph beginning on page 16, line 22, with the following rewritten paragraph:

-- However, in order to further reduce immunogenicity, it was elected to PRIMATIZE® two primate monoclonal antibodies (a type of chimerization of antibodies) according to the methodology which is also described in U.S. Serial No. 08/379,072 ~~(now allowed)~~ (U.S. Patent No. 5,658,570), which is incorporated by reference herein.

PRIMATIZATION® essentially refers to the production of recombinant antibodies developed by IDEC Pharmaceuticals Corporation which comprise primate variable regions and human constant regions. ~~Primatization~~ PRIMATIZATION® of the two primate anti-human CD23 monoclonal (5E8 and 6G5) antibodies having potent IgE inhibiting activity was effected in order to eliminate any potential immunogenicity attributable to the primate constant domains in humans. --

Please replace the paragraph beginning on page 19, line 32, with the following rewritten paragraph:

-- A particularly preferred vector system is the translationally impaired vector system disclosed in U.S. Serial No. 08/147,696 ~~(now allowed)~~ which issued as U.S. Patent No. 5,648,267 on July 15, 1997, which comprises a translationally impaired dominant selectable marker (neo) containing an intron into which a desired heterologous DNA is inserted. This vector system has been found to provide for very high yields of recombinant proteins, e.g., immunoglobulins. However, the subject anti-CD23 antibodies may be produced in any vector system which is suitable for expression of functional immunoglobulins. --

Please replace the paragraph beginning on page 20, line 9, with the following rewritten paragraph:

-- Also, the present invention embraces human monoclonal antibodies of the gamma-1 or gamma-3 types which are specific to human CD23. Methods for isolation of human monoclonal antibodies are also well known in the art and include *in vitro* methods, e.g., *in vitro* immunization of human B cells in tissue culture, and *in vivo* methods, e.g. synthesis of human monoclonal antibodies in SCID mice. A preferred means of producing human monoclonal antibodies in SCID mice which combines *in vitro* priming of human spleen cells which are then introduced into SCID mice is disclosed in U.S. Serial No. 08/488,376 which issued as U.S. Patent No. 5,811,524 on September 22, 1998 (incorporated by reference in its entirety herein). This method is advantageous as it provides for the reproducible recovery of monoclonal antibodies having high affinity against a desired antigen, e.g., a human antigen. --

Please replace the paragraph beginning on page 20, line 31, with the following rewritten paragraph:

-- Five primate monoclonal antibodies specific to CD23 were isolated from macaques substantially according to the methodology disclosed in Serial No. 08/379,072 (U.S. Patent No. 5,658,570), which has been incorporated by reference herein. The exact techniques utilized are described in detail below. --

Please replace the paragraph beginning on page 21, line 7, with the following rewritten paragraph:

-- During purification, soluble CD23 (sCD23) was quantified by a three-step ELISA using a murine anti-CD23 antibody (Binding Site; catalog # MC112) as a capture. The antigen was partially purified from cultures of 8866 cells maintained in suspension bioreactors using RPMI 1640 (JRH Biosciences; catalog # 56-509) supplemented with 10% fetal bovine serum (JRH Biosciences) and 4 mM glutamine (JRH Biosciences; catalog # 90114) at 37°C. Carbon dioxide was used to maintain pH 7.1. After removing cells by 0.45 μm filtration, phenylmethyl sulfonyl fluoride (final concentration 0.2 mM, ~~Sigman~~ Sigma Chemical Co.; catalog # P-7626) and ethylenediaminetetraacetic acid (final concentration 3 mM, Sigma Chemical Co.; catalog # EDS) were added to the supernate and the solution stored at 2-8°C. The cell-free supernate was concentrated approximately 15 to 20-fold using a hollow-fiber ultrafiltration cartridge (A/T Technology; catalog # UFP-10-C-9A; 10,000 d MWCO) or tangential flow ultrafiltration cartridge (Filtron Corporation; 10,000 d MWCO) at ambient temperature. The concentrated supernate was sterile filtered and stored at -70°C. Thawed concentrates were de-lipidated by adding SM-2 BioBeads (BioRad Industries; catalog # 152-3920) at 5 g/L and stirring overnight at 2-8°C. The resin was removed by filtration and the solution stored at 2-8°C. For some preparations of sCD23, concentrates were fractionated using ammonium sulfate (35-70% (w/v); Fisher; catalog # A702-3) before or after de-lipidation. --

Please replace the paragraph beginning on page 37, line 27, with the following rewritten paragraph:

-- A modified SCID mouse model was used because it is known that severe combined immunodeficiency scid/scid (SCID) mice, C.B.-17 (Bosma et al., *Nature*, 301:527 (1983)) reconstituted with human peripheral blood mononuclear cells (hu-PBMC-SCID) can produce significant quantities of human immunoglobulins (Ig) (~~Moiser~~ Mosier et al., *Nature*, 335:256 (1988); ~~Moiser~~ Mosier et al., *J. Clin. Immunol.*, 10:185 (1990); Abedi et al., *J. Immunol.*,

22:823 (1992); and Mazingue et al., *Eur. J. Immunol.*, 21:1763 (1991).) The predominant isotype of human immunoglobulin (Ig) produced in hu-PBMC-SCID mice is IgG. Generally, IgM, IgA and IgE isotypes are found in very low or non-detectable levels except in cases where PBMC is obtained from donors with certain autoimmune or allergic disease conditions. It has also been reported that manipulation of hu-PBMC SCID mouse model with certain cytokines may be provided for the generation of significant levels of non-IgG isotypes, including IgE (Kilchherr et al., *Cellular Immunology*, 151:241 (1993); Spiegelberg et al., *J. Clin. Investigation*, 93:711 (1994); and Carballido et al., *J. Immunol.*, 155:4162 (1995)). The hu-PBMC-SCIDs, has been also used to generate antigen specific Ig provided the donor has been primed for the antigen *in vivo*. --

Please replace the paragraph beginning on page 59, line 18, with the following rewritten paragraph:

-- Numerous methods exist for conversion of murine antibodies to chimeras in which the heavy and light chain constant regions are substituted with human versions or in which all but the CDRs (complementary determining regions) are substituted with their human equivalents. (See King et al., Biochem. J. 281:317-23, 1992; Queen et al., Proc. Nat. Acad. Sci. USA 86(24):10029-33, 1989; Love et al., Methods Enzymol. 178:515-27, 1989; Hutzell et al., Cancer Res. 51:181, 1991; Chiang et al., Biotechniques 7(4):360-6, 1989; Heinrich et al., J. Immunol. 143:3589, 1989; Hardman et al., Int. J. Cancer 44:424, 1989; Orlandi et al., Proc. Nat. Acad. Sci. USA 86(10):3833-6, 1989). --

Please replace the paragraph beginning on page 78, line 1, with the following rewritten paragraph:

-- Of these, the preferred indications treatable or presentable by administration of anti-CD23 antibodies include allergic rhinitis and conjunctivitis, atopic dermatitis; eczema; Job's syndrome, asthma; allergic conditions; and chronic inflammatory diseases and conditions, including CLL chronic lymphocytic leukemia, typically characterized by high levels of membrane CD23 and high circulating levels of sCD23 (~~Sarfart~~ Sarfati et al., Blood 71: 94-98 (1988)). --